REMARKS

STATUS OF THE CLAIMS

Claims 1-9, 11 and 21-23 were pending in the application. Claims 21 – 23 have been canceled in this amendment. Claims 10 and 12 – 20 have been withdrawn by the USPTO as being drawn to non-elected species. Claim 1 has been amended. New claims 24 – 30 have been added. Claims 1 – 9, 11, and 24 – 30 would be pending in the application if the instant amendment is entered.

New claims 24 – 30 are of the same claim scope as claims 3 – 9 but are dependent upon claim 2 rather than claim 1. Claim 2 limits the compound of claim 1 to ospemifene. Therefore, no new matter is submitted.

Reconsideration and re-examination of this application in view of the above amendments and the following remarks is herein respectfully requested.

REJECTION OF CLAIMS 1-9 AND 11 UNDER 35 U.S.C. §102(e)

Claims 1-9 and 11 stand rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Application No. 2005/0215528 ("Furuya"). Furuya teaches a pharmaceutical composition for preventing or treating a series of diseases such as breast cancer, menopausal syndrome, precocious puberty, etc., wherein the composition is a combination of a GnRH agonist and a SERM, SARM, sex hormone synthesis inhibitor, recetpro-type tyrosine kinase inhibitor, bone metabolism modifier, immunotherapeutic drug, cytokine/chemokine inhibitor or an endothelin receptor antagonist. The Examiner maintains that the composition disclosed in Furuya may be a solid drug formulation comprising granulates of ospemifene which also may contain intragranular excipients, disintegrants, binders, excipients, caboxymethylcellulose, lactose, dextrin, etc., and may be made by wet granulation. The Examiner confirms that Furuya does not teach particle size limitations.

Without acquiescing to the rejection, Applicants submit that with the amendments to claim 1 adding the particle size range and the dissolution profile, this rejection is deemed to be overcome. Regardless of the amendments, Applicants point out that these amendments are not necessary to overcome an anticipation rejection since the Examiner is picking and choosing several variables from a broad generic disclosure in an attempt to arrive at Applicant's specific formulation.

Therefore, since the rejection of claims 1 – 9 and 11 in light of Furuya is obviated by the amendments, Applicants respectfully requested reconsideration and withdrawal.

REJECTION OF CLAIMS 1 AND 21-23 UNDER 35 U.S.C. §103(a)

Claims 1 and 21 – 23 stand rejected as being unpatentable over Furuya. In light of now canceled claims 21 – 23, this rejection is deemed to be moot. In light of claim 1, as amended, this rejection is respectfully traversed.

Furuya teaches a pharmaceutical composition for preventing or treating a series of diseases such as breast cancer, menopausal syndrome, precocious puberty, etc., wherein the composition is a combination of a GnRH agonist and a SERM, SARM, sex hormone synthesis inhibitor, receptor-type tyrosine kinase inhibitor, bone metabolism modifier, immunotherapeutic drug, cytokine/chemokine inhibitor or an endothelin receptor antagonist.

A finding of obviousness requires that the prior art both suggest the invention and provide one of ordinary skill with a reasonable expectation of success. *In re O'Farrell* 853 F.2d 894, 903, 7 USPQ2d 1673 (Fed. Cir. 1988). Secondary considerations such as unexpected results must be considered if present. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538-39, 218 USPQ 871, 879 (Fed. Cir. 1983); *In re Merck & Co., Inc.*, 800 F.2d 1091, 1096, 231 USPQ 375, 378 (Fed. Cir. 1986). In this case, Applicants' formulation comprising a granulated form of ospemifene of a specific particle size range is not suggested by the prior art and achieves unexpected results.

First, Applicants submit that the claimed invention as amended is not *prima facie* obvious. There is nothing in Furuya to suggest ospemifene of a particular, discreet particle size range (i.e., wherein 90% of the particles have a size less than 50 micrometers and 50% of the particles have a size less than 15 micrometers) in granulated form wherein at least 80% of the formulation is dissolved within 30 minutes after subjecting said formulation to dissolution testing at pH 9.8 according to the USP 24 paddle method.

Second, the invention possesses unexpected results. Applicants' unexpected results lie in the discovery that when ospemifene of a particular, discreet particle size range (i.e., wherein 90% of the particles have a size less than 50 micrometers and

50% of the particles have a size less than 15 micrometers) is granulated, it possesses a far superior *in vitro* dissolution profile over tablets of ospemifene made by direct compression techniques. As seen in Figure 1 in the specification, the particular granulated formulation claimed herein shows greater than 80% dissolution in the particular *in vitro* dissolution tests and substantially complete dissolution within two hours. In contrast the ospemifene tablets made by direct compression show approximately 60% dissolution at the thirty minute mark and no more than 80% dissolution at the two hour timepoint.

The Examiner cites *In re Aller*, 220 F.2d 454, 456; 105 USPQ 233, 235 (CCPA 1955) for the proposition that where general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. However, not all of the claimed conditions in the amended claims have been disclosed in the prior art. For example, in *Heller* the prior art disclosed a process for decomposing isopropyl benzene hydroperoxide and provided a working example where the process was conducted at a temperature of 100° C and with a 10% sulphuric acid solution. The appellants attempted to claim an identical process except that the temperatures were lower and the sulphuric acid concentrations were higher than the prior art reference. However, the appellants did not appear to show actual improved results over the prior art reference (phenol yields 83.7% v. 75%; 71% v. 60% acetone yields, although prior art silent; reaction times of 20 min to 3 hours v. 1.5 hour reaction times).

The CCPA stated that "[n]ormally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art." *Aller* at p. 235.

First, with regard to *Aller*, it should be noted that with "such 'rules of patentability' (and the ever-lengthening list of exceptions which they engender) is that they tend to becloud the ultimate legal issue – obviousness – and exalt the formal exercise of squeezing new factual situations into preestablished pigeonholes. Additionally, the emphasis upon routine experimentation is contrary to the last sentence of section 103." *In re Yates*, 663 F.2d 1054, 1056 (CCPA 1981).

In the instant case, as admitted by the Examiner, there is nothing in Furuya disclosing possible particle size ranges. There nothing suggesting how the granulation of ospemifene of a discreet particle size range could improve the *in vitro* dissolution in the manner shown in the instant invention. Furuya discloses thousands of active ingredients and a large generic disclosure of pharmaceutical excipients to solve a different problem, e.g. improving the preventative or therapeutic effect of a GnRH agonist on various diseases and improving the quality of life of the patient. In short, there is no teaching or suggestion of the claimed invention as amended.

Therefore, Applicants submit that the claimed invention, as amended, is patentable over Furuya and respectfully request reconsideration and withdrawal of the obviousness rejection.

REJECTION OF CLAIMS 1-9, 11, AND 23 FOR OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 1 – 9, 11, and 21 – 23 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 - 12 of copending Application No. 11/592,989 ('989 application). The Examiner argues that the claims are patentably indistinct because the '989 application claims a drug formulation comprising ospemifene. Applicants disagree and respectfully traverse the rejection.

The '989 application discloses a composition that relate to semi-solid or liquid formulations including solutions, gels, pastes, etc. In contrast, the present invention teaches a solid drug formulation comprising granulates containing ospemifene in particulate form wherein 90% of the particles have a size less than 50 micrometers and 50% of the particles have a size less than 15 micrometers in combination with one or more intra-granular excipients, wherein at least 80% of the formulation is dissolved within 30 minutes after subjecting said formulation to dissolution testing at pH 9.8 according to the USP 24 paddle method. According to the Examiner's own reasoning, this is a patentably distinct invention. Applicants point out that the Examiner has already determined that a formulation of the present invention made by wet granulation is patentably distinct from a formulation made by dry granulation. Clearly, an ospemifene formulation that is solution or semi-solid is patentably distinct from a solid formulation of ospemifene in particulate form having a discreet particle

size range and being granulated to improve *in vitro* dissolution. For the sake of consistency, Applicants request that the provisional rejection of the claims be reconsidered and withdrawn.

Applicants thank the Examiner for his consideration of this case and submit that the case is in condition for immediate allowance. If the Examiner believes that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at 734-302-6042.

Respectfully submitted,

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